Appln. No. 10/807,620

Amendment dated July 1, 2009

Reply to Office Action of January 5, 2009

The listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims:

Claims 1-21. (cancelled).

Claim 22. (Currently amended) A kit for carrying out the combined administration of suramin with one or more cytotoxic agents, comprising:

- (a) suramin formulated in a pharmaceutical carrier; and
- (b) a cytotoxic agent being one or more of an anti-microtubule agent, a topoisomerase I inhibitor, a topoisomerase II inhibitor, an anti-metabolite, a mitotic inhibitor, an alkylating agent, an intercalating agent, an agent capable of interfering with a signal transduction pathway, an agent that promotes one or more of apoptosis or necrosis, an interferon, an interleukin, or a tumor necrosis factor, or radiation; and
- (c)\(\frac{1}{2}\) instructions for therapeutic use of said suramin in combination with said cytotoxic agent(s) in one or more of inhibiting growth, proliferation of tumor cells, or inducing killing of tumor cells, calling for:
 - (i) administering suramin, if required, in a required dose to establish a low circulating concentration of suramin in said patient of below about 200 μM; and
 - (ii) administering said chemotherapeutic agent to said patient when said low circulating concentration of suramin of below about 200 μM is present in said patient,-

wherein the required dose of suramin can be is determined in step (c) (b) by the steps of:

- (bc1) determining the squared value of the body surface area (BSA) of said patient;
- (bc 2) determining the time elapsed, in days, since the initiation of the last suramin treatment; and
- (bc 3) calculating the dose of low dose suramin using a nomogram that shows the dose according to the parameters of squared value of body surface, and elapsed days since last suramin treatment.

said nomogram comprising:

Nomogram For Calculating Suramin Dose

Cycle 1*	<u>125</u>
Days since the administration of the first dose of previous cycle	<u>FACTOR</u>
<u>7</u>	<u>39</u>
<u>8</u>	<u>43</u>
<u>9</u>	<u>47</u>
<u>10</u>	<u>51</u>
<u>11</u>	<u>55</u>
<u>12</u>	<u>58</u>
<u>13</u>	<u>61</u>
<u>14</u>	<u>64</u>
<u>15</u>	<u>67</u>
<u>16</u>	<u>69</u>
<u>17</u>	<u>72</u>
<u>18</u>	<u>74</u>
<u>19</u>	<u>76</u>
<u>20</u>	<u>78</u>
<u>21</u>	<u>80</u>
<u>22</u>	<u>82</u>
<u>23</u>	<u>84</u>
<u>24</u>	<u>86</u>
<u>25</u>	<u>87</u>
<u>26</u>	<u>88</u>
<u>27</u>	<u>90</u>
<u>28</u>	<u>91</u>

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<u>29</u>	<u>92</u>
<u>30</u>	<u>93</u>
<u>31</u>	<u>94</u>
<u>32</u>	<u>95</u>
<u>33</u>	<u>96</u>
<u>34</u>	<u>97</u>
<u>35</u>	<u>98</u>
<u>36</u>	<u>98</u>
<u>37</u>	<u>99</u>
<u>38</u>	<u>100</u>
<u>39</u>	<u>100</u>
<u>41</u>	<u>102</u>
<u>42</u>	<u>102</u>
44	<u>103</u>
<u>47</u>	<u>104</u>
<u>49</u>	<u>105</u>
<u>52</u>	<u>106</u>
<u>55</u>	<u>106</u>

where:

First cycle dose (mg) =
$$\frac{(21.4*5.13*BSA^2)}{e^{-(0.0026 \text{ or } 0.0022*48)}}$$
 = 125*BSA² Eq. 15

<u>and</u>

Subsequent cycle dose (mg) = First dose *
$$(1-e^{-k^* t})$$
 = $125*BSA^{2*}$ $(1-e^{-k^* t})$ = $FACTOR*BSA^2$ Eq. 16 wherein

"BSA" is body surface area in units of m²,

"k" is the rate constant of decline of suramin concentrations in plasma in units of 1/hour,

"t" is time after suramin administration in units of hours

Claims 23, 24 and 25. (cancelled)

Claim 26. (Original) The kit of claim 22, wherein one of the cytotoxic agents is <u>one or more of</u> carboplatin_paclitaxel, docetaxel, gemcitabine, or 5-fluorouracil.

Claim 27. (Previously presented) The kit of claim 22, wherein said low circulating concentration of suramin is between about 10 and 200 µM.

Claim 28. (Previously presented) The kit of claim 27, wherein said low dose of circulating suramin is between about 10 and 50 μ M.

Cancel Claims 29, 30, and 31.

Claim 32. (Previously presented) The kit of claim 22, wherein a suramin dose is administered such that a concentration of between about 10 to about 50 µM over 48 hours is achieved in a patient.

Claim 33. (Previously presented) The kit of claim 22, wherein two-thirds of the therapeutically effective amount of suramin is given on the first day and the remaining one-third of the therapeutically effective amount of suramin is given about 24 hours later.

Claim 34. (Previously presented) The kit of claim 22, wherein a suramin dose greater than a low dose suramin is administered to a patient and a chemotherapeutic agent thereafter is administered to said patient only after a suramin plasma concentration of between about 10 to about 50 µM is achieved in said patient.